

#### **VIII-A. Scientific Abstract**

This is a Phase I study of the delivery of a replication-defective recombinant adenovirus containing the herpes simplex virus (HSV) thymidine kinase (tk) gene (AdV.RSV-tk) to the peritoneal cavity of patients with recurrent ovarian cancer after optimal tumor debulking (residual <2 cm in diameter) and followed by concomitant intravenous administration of acyclovir and topotecan. The AdV.RSV-tk adenovirus vector will be prepared in the Gene Vector Laboratory at Baylor College of Medicine. The AdV.RSV-tk virus has been approved by the Baylor IRB and the FDA for treating human brain tumors and prostate cancer. Acyclovir is approved for the treatment of chicken pox, recurrent mucosal, cutaneous HSV-1 and HSV-2, varicella-zoster infection in immunocompromised patients, herpes simplex encephalitis and genital herpes. Topotecan demonstrated broad anti-tumor activity in pre-clinical studies. Topotecan shows clinical activity against cisplatin-refractory ovarian cancer with an expected response rate of 18-24%, which is one of the highest activities of any chemotherapeutic agents against this disease today. If topotecan is used in combination with adenovirus-mediated gene therapy, a synergistic effect of cell-killing can be expected, according to our pre-clinical data. The primary objective is to evaluate the safety of this therapy, the maximum dose of adenovirus, and the dose-limiting side effects. A secondary objective will be to evaluate the clinical effectiveness of this therapy on the residual ovarian cancer with or without malignant ascites. Also, 30 days after treatment, a laparotomy or laparoscopy will be performed to harvest tumor tissue and uninvolved peritoneum for molecular studies of treatment effects.